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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/728,173	12/01/2000	Keisuke Kuida		4567

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James F. Haley, Jr.
C/O FISH & NEAVE IP GROUP
ROPES & GRAY LLP
1251 Avenue of the Americas
New York, NY 10020

EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/728,173	KUIDA ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5 and 8-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 8/31/2005 is acknowledged. Claims 1,3-5, and 8-11 are pending. Claims 2,6 and 7 were canceled, claims 1and 3-5 were amended. Claims 1,3-5, and 8-11 are under consideration. The sections of 35 U.S.C. not included in this office action can be found in a previous office action. An action on the merits follows.

Specification

The objection to the specification because the Brief Description of the Drawings does not match the drawings submitted on 12/01/2000, is withdrawn in response to applicant's amendments to the specification

Claim Rejections - 35 USC § 101

The rejection of Claims 1-5 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in response to applicant's amendments to the claims.

Claim Rejections - 35 USC § 112

The rejection of amended and new claims 1, 8 and 9 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The rejection of claims 3-5 is withdrawn in view of applicant's amendment to the claims.

The rejection of amended, original and new claims 1,3-5,8-11 under 35 U.S.C. 112, first paragraph, is maintained, because the specification, while being enabling for a transgenic mouse whose genome comprises a homozygous disruption in an endogenous Caspase-9 gene, wherein said mouse lacks functional Caspase-9 expression and exhibits CNS abnormalities including hypercellularity and ventricular hypertrophy, a transgenic mouse whose genome comprises a heterozygous disruption in an endogenous Caspase-9 gene, wherein said mouse lacks functional Caspase-9 expression from the disrupted endogenous Caspase-9 gene, and a method of making said mice via homologous recombination of an isolated DNA sequence comprising a genomic DNA sequence encoding a disrupted mouse Caspase-9 gene with an endogenous mouse Caspase-9 gene, does not reasonably provide enablement for any genetically altered mouse defective in Caspase-9 expression or a method of making any such animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Response to Arguments

Applicant's arguments filed 8/31/2005 have been fully considered but they are not persuasive. Applicant argues that the claims have full written description since claim 1 was amended to read on a genetically altered mouse defective in Caspase-9 expression *due to a effective Caspase-9 gene*. However, the claims continue to be drawn to a genetically altered mouse defective in Caspase-9 expression. The claims encompass any mouse that has been

genetically altered in any way that causes defective Caspase-9 expression. The claims encompass a genus of genetically altered mice that are defined solely by a defect in Caspase-9 expression. As applicant's note: "defective" means "imperfect in form or function." The term defective encompasses any gain or loss of function. Therefore the present claim encompasses a genus of mice that completely lack Caspase-9 expression, to mice that vastly overexpress endogenous Caspase-9. As previously stated: the specification only discloses a mouse defective in Caspase-9 expression due to the disruption of an endogenous Caspase-9 gene, by replacement of the QACXG pentapeptide motif with a *neo* sequence. This mouse is substantially different from and does not adequately describe a mouse that is defective because of an increase in Caspase-9 expression or because of a gain-of-function mutation in the Caspase-9 gene.

Applicant argues that it was common knowledge in the art at the time of filing that there was a substantial number of ways of rendering a gene defective. Applicant then lists several of these methods. Applicant should note that that this is not an enablement rejection. The examiner acknowledges that there were multiple known methods of rendering a gene defective at the time of filing. The issue is whether the applicant has adequately described the full genus of applicant's claimed invention as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This invention as presently claimed encompasses any mouse with a defective Caspase-9 gene, which includes an increase or decrease in Caspase-9 expression. The disclosure of a single species of a Caspase-9 knockout mouse is not considered to be sufficient to describe the claimed genus of "defective" mice. Thus, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for any genetically altered mouse defective in Caspase-9 expression. For the

reasons of record stated, above and in the previous action of 8/31/2005, the rejection over this issue is maintained.

Applicant argues that amending the claims to clarify that the defect in Caspase-9 expression results from a defective Caspase-9 gene they have rendered the Examiner's concerns about transgenic animals expressing Caspase-9 regulators moot. This is not found to be persuasive. Applicant's claims continue to encompass any defective Caspase-9 gene, which encompasses both gain of function mutations as well as disruptions in Caspase-9 function causing partial or full absence of functional Caspase-9 expression. As stated previously the only mouse disclosed in the specification is a transgenic knockout mouse, wherein the *neo* gene cassette was integrated into the Caspase-9 gene by homologous recombination. While the specification teaches how to make a heterozygous knockout mouse and a homozygous knockout mouse, it is noted that the only known use of the heterozygous mouse is to breed the homozygous knockout mouse. This is because the heterozygous knockout mouse has no disclosed phenotype that differs from a wild-type mouse. Further, applicant's claims encompass a transgenic mouse with any defective Caspase-9 gene, including a mouse with a trivial point mutation leading to slight decrease in Caspase-9 expression. However, the only mouse with the disclosed phenotype of CNS abnormalities including hypercellularity and ventricular hypertrophy is a mouse homozygous for the disruption of the endogenous Caspase-9 genes. Finally, the method of making a transgenic mouse in claim 3 does not require homologous recombination of SEQ ID NO:7 with the endogenous Caspase-9 gene. It is unclear how this method can be used to make the claimed mouse if the sequence stably integrates at another site within the genome, since this will not disrupt the endogenous Caspas-9 gene and will not

produce the disclosed phenotype. Applicant has provided no guidance that it is possible to produce the phenotype of the disclosed homozygous knockout mouse with any other mutations.

Applicant's arguments regarding Tri-lox technology, enablement for strains other than C57BL/6 and mutations other than knocking out the QACXG sequence were found persuasive and the scope of enablement has been altered accordingly. However, it is again noted that applicant is only enabled for transgenic mice (homozygous and heterozygous) with disruptions of the endogenous Caspase-9 gene leading to a total absence of function of the disrupted gene. For the reasons of record stated, above and in the previous action of 8/31/2005, the rejection over this issue is maintained.

Rejections under the second paragraph of 35 U.S.C. 112:

The rejection of claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of applicant's amendments to the claims.

No Claims Allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Dr. Louis D. Lieto
Patent Examiner
Art Unit 1632

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1630